Asian Journal of Medical and Pharmaceutical Sciences
https://doi.org/10.30904/j.ajmps.2026.4930 | E-ISSN: 2348-0165

A Review on Bubonic Plague, Pathogenesis and Its Preventive and Treatment Approaches

Arava Vidhyadhari*[1], Erri Kalyan[2], Gottiganti Jaswanth[2], Konduru Ravi Kumar[2], S. Arun[2], Salivindula Narasimhulu[2], Kommeri Nandabaskar[2], Chinta Sudharani[2], Mogali Haritha[2], Sura Rajini[2]

[1]*Department of Pharmacology, Saastra College of Pharmaceutical Education and Research, Varigonda, T.P Gudur, Nellore.*
[2]*B.Pharm student, Saastra College of Pharmaceutical Education and Research, Varigonda, T.P Gudur, Nellore.*
***Corresponding E-mail:** aravavidhyadhari@gmail.com*

Received: 29 Jan 2026 | Revised: 11 Feb 2026 | Accepted: 28 Feb 2026 | Published: 23 March 2026

Abstract:
An ancient disease, its bacterial agent (Yersinia pestis) still causes periodic outbreaks and remains endemic in some parts of the world. Additionally, because it could be weaponized for world bioterrorism, understanding its clinical syndromes, epidemiology, and treatment options remains critical for medical practitioners. Finally, recent molecular discoveries linking recessive familial Mediterranean fever mutations to plague immunity have revolutionized how scientists and historians alike view this novel evolutionary adaptation. Y.pestis is an aerobic, gram-negative coccobacillus in the family Enterobacteriaceae. Genetic DNA analysis shows that it diverged from its enteric pathogenic relative, Yersinia pseudotuberculosis, up to 6000 years ago. After incubation for 24 to 48 hours in blood. Its primary vector for transmission is the Xenopsylla cheopis flea, although roughly 80 species of fleas can carry it. During the Black Death, the flea was transported by the black rat or Rattus. The clinical forms of the plague include high fevers, terrible pains in their limbs and abdomen, and headaches generally between 3 and 7 days after exposure. The bacteria reproduce rapidly in lymph nodes located closest to the flea bites, leading to painful swellings in the groin, cervical, axillary lymph nodes, which can enlarge to the size of an egg. The modern medicine has greatly improved therapies can prevent the future consequences of infection among the people.

Keywords: Yersinia pestis, Mediterranean fever, Immunity, Modern medicine, Infection

Introduction

Killing more than 25 million people or at least one third of Europe's population during the fourteenth century, the Black Death or bubonic plague was one of mankind's worst pandemics, invoking direct comparisons to our current coronavirus "modern plague." An ancient disease, its bacterial agent (Yersinia pestis) still causes periodic outbreaks and remains endemic in some parts of the world. Additionally, because it could be weaponized for world bioterrorism, understanding its clinical syndromes, epidemiology, and treatment options remains critical for medical practitioners[1-2].

History of Plague

The plague has afflicted humanity for thousands of years. Molecular studies identified the presence of the Y. pestis plague DNA genome in 2 Bronze Age skeletons dated at roughly 3800 years old. In the biblical book 1 Samuel from approximately 1000 BCE, the Philistines experience an outbreak of tumors associated with rodents, which might have been bubonic plague. Scholars identify 3 plague pandemics. The first pandemic or Justinian plague probably came from India and reached Constantinople in 541-542 CE. At least 18 waves of plague spread across the Mediterranean basin into distant areas like Persia and Ireland from 541 to 750 CE. In Europe, plague-stricken citizens were often dead within a week of contracting the illness. Ultimately, at least one third of the European population (more than 25 million people) died between 1347 and 1352 from the Black Death. The plague spread to France and Spain in 1348 and then to Germany, Switzerland, and Austria. It decimated London in 1349 and reached Scandinavia and northern England by 1350. The plague died out by the century's end, but outbreaks resurfaced and spread throughout Europe over the next 400 years. In 1656-1657, two thirds of the population in Naples and Genoa died from the disease. In 1665-1666, London lost about one quarter of its citizens to plague, about 100,000, and the same number died in Vienna in 1679[3-4].

Causes

Bacteria Agent: Yersinia pestis is the confirmed causative agent, often carried by fleas that infested black rats.

Transmission Vectors: While fleas on rodents were the main culprits, the plague also spread through contact with infected body fluids/tissues and, in the case of pneumonic plague, via human-to-human respiratory droplet transmission

Types of Plague: The pandemic manifested in three forms: bubonic (lymph node infection), septicemic (blood infection), and pneumonic (lung infection).

Environmental Factors: The outbreak was exacerbated by existing factors such as famine, war, and the end of the Medieval Warm Period, which weakened the population.

Risk Factors

Geographic Location and Travel: Residing in or traveling to regions where plague is endemic, such as parts of Africa, Asia, and the western United States (e.g., rural areas, high-altitude regions).

Flea Bites (Primary Transmission): Bites from infected fleas, particularly the Oriental rat flea (Xenopsylla cheopis), are the most common source of infection.

Handling Infected Animals:

Direct contact with tissues or fluids from infected animals including rodents, rabbits, hares, and pets can transmit the

bacteria through skin breaks. Hunters and veterinarians are at higher risk.

Pet Exposure: Dogs and, more commonly, cats can bring infected fleas into the home or develop the disease themselves.

Environmental Factors: Living in or visiting areas with poor sanitation, overcrowded conditions, or high rodent populations (epizootics).

Occupational Hazards: Occupations that involve outdoor work in endemic areas, such as farming, field biology, or veterinary work.

Weakened Immune System: Individuals with underlying conditions like HIV/AIDS or cancer may be more susceptible to severe illness.

Epidemiology

Plague is a disease caused by infection with the bacterium Yersinia pestis, usually found in small mammals and their fleas. It is no longer found in the UK, but occurs in several countries in Africa, Asia, South America, and in the USA. Since the 1990s, most human cases have occurred in Africa, with the Democratic Republic of Congo (DRC) and Madagascar considered to be the most highly endemic countries. Madagascar experiences regular seasonal outbreaks, but to date there have been no known exported cases[5-6].

Transmission

Rodents are the main reservoir of infection. Yersinia pestis can be transmitted to humans in a number of ways, including through bites from infected rodent fleas or from handling infected animals or their tissues. In higher income countries, sporadic infections may be caused by exposure to infected cats (via fleas, scratches or bites) who have acquired infection from interactions with wild rodents. Laboratory exposure may also occur. Another important route of transmission is through the inhalation of infectious respiratory particles from a patient with pneumonic plague. This usually requires close and prolonged contact with the patient. Humans have also been infected via the respiratory secretions of infected cats.

Symptoms: There are 3 main forms of plague depending on the route of infection: bubonic, pneumonic and, more rarely, septicaemic. Other forms such as meningitis and pharyngitis are seen but are rare.

Bubonic plague

Bubonic plague is the most common form of plague and is usually caused by the bite of an infected flea. The bacteria travel from the site of the bite to local lymph nodes which become inflamed and painful. This is called a bubo. Patients usually present 2 to 8 days after exposure with fever, headache, chills and buboes. If this form of infection is not treated, the bacteria can then spread to the lungs, meninges or bloodstream.

Pneumonic plague

Pneumonic plague is the rarest and also the most severe form of plague. It may result from spread to the lungs from advanced bubonic plague but is more usually due to inhalation of infectious particles. Person-to-person transmission is seen but the degree of contact needed is not clear. Patients present with a rapidly developing pneumonia and may produce bloody sputum. Untreated pneumonic plague is almost always fatal. Even with prompt recognition and treatment, mortality is around 30%.

Septicaemic plague

Septicaemic plague occurs when infection spreads through the bloodstream. This may be a progression of untreated bubonic plague in 10 to 20% of cases or can occur as the primary infection. It causes a sepsis syndrome with bleeding, tissue necrosis and shock. Patients may also have non-specific symptoms such as abdominal pain, nausea and vomiting, and diarrhoea. Untreated, septicaemic plague results in disseminated intravascular coagulation and microthrombi formation. Bubonic plague, caused by Yersinia pestis, begins when infected fleas regurgitate bacteria into the skin during a blood meal. The bacteria migrate to local lymph nodes, replicating rapidly to cause painful, necrotic swellings called buboes. Y. pestis suppresses the immune response and disseminates via blood, often leading to sepsis, secondary pneumonia, high mortality if untreated.

Pathogenesis Stages:

Transmission and Entry: Y. pestis is transmitted by the bite of an infected flea, which carries the bacteria in its blocked foregut. A single bite can introduce thousands of bacteria.

Immune Evasion:

Initially, bacteria are phagocytosed by macrophages and monocytes but manage to survive and multiply within them. They resist phagocytosis through specialized virulence factors (e.g., F1 capsule antigen, pH 6 antigen).

Lymphatic Migration (Bubo Formation):

Bacteria travel through lymphatics to the nearest lymph node. The node becomes extremely inflamed, tense, and painful, known as a bubo. Tissue within the lymph node becomes necrotic and hemorrhagic.

Systemic Dissemination:

Bacteria escape the lymph nodes and enter the bloodstream, leading to septicemic plague. Y. pestis spreads to organs like the spleen, liver, and lungs.

Secondary Infection:

The bacteria can infect the lungs, leading to secondary pneumonic plague, which allows for human-to-human transmission via droplets.

Laboratory test:

Rapid Diagnostic Test: A highly sensitive, 15-minute lateral flow dipstick test that detects the F1 antigen in bubo aspirate, serum, or sputum.

Microscopic Examination:

Smears of fluid from lymph nodes or blood stained with Wayson, Wright, or Giemsa stains show bacteria with a characteristic "safety pin" appearance.

Bubo Aspirate Culture:

The "gold standard" for confirmation, identifying Y. pestis from the swollen lymph node.

PCR Assay:

Molecular testing (polymerase chain reaction) to detect Y. pestis DNA, often used for fast, specific confirmation7-10.

Serology:

Blood tests to detect antibodies (anti-F1) in serum, often used for retrospective diagnosis (comparing acute and convalescent phases).

Treatment

First-Line Drugs: Gentamicin or Streptomycin (often preferred for severe cases).

Alternative/First-Line Oral Drugs:

Ciprofloxacin, Levofloxacin, Moxifloxacin, and Doxycycline.

Duration: Typically 10 to 14 days, or until the patient has been afebrile for 2-3 days.

Treatment Timing: Urgent care is required; antibiotics should be started immediately if plague is suspected, even before laboratory confirmation11-12.

Supportive Care: Hospitalization is required, sometimes involving intravenous fluids, respiratory support, and surgical drainage of lymph nodes.

Prevention Control Fleas on Pets: Use flea products on pets, especially if they roam outside in areas where plague is found.

Rodent-Proof Your Home: Remove brush, wood piles, and food sources that attract mice and squirrels.

Avoid Wild Animals: Do not handle sick or dead animals. Wear gloves if handling wildlife, such as when hunting.

Use Insect Repellent: Use repellent containing DEET on skin and clothing to prevent flea bites when hiking or camping.

Seek Immediate Medical Care: If you develop a fever, chills, or swollen lymph nodes after potential exposure, contact a doctor immediately.

Travel and High-Risk Situations

Travelers: While risk is low for most travelers, avoid rat-infested areas, particularly where dead rodents have been reported.

Prophylactic Antibiotics:

If you have been directly exposed to fleas or a sick animal, a doctor may recommend short-term antibiotic treatment.

Vaccination:

A plague vaccine exists but is generally recommended only for high-risk individuals, such as laboratory personnel or health care workers, not the general public13-14.

Conclusion

Bubonic plague prevention relies on controlling rodent populations, using flea repellent, and ensuring rapid diagnosis and antibiotic treatment, as prompt medical care is critical to positive outcomes. Modern public health measures focusing on sanitation and early intervention are essential to control the disease, which remains a threat in certain areas. Plague represents a reemerging infectious disease with potential use for bioterrorism. From prehistory to the modern era, Y. pestis has killed millions of people. Outbreaks of worldwide plague foci in both developed and underdeveloped countries continue to occur. Although modern medicine has greatly improved therapies and limited its spread, many clinical practitioners remain unfamiliar with its symptomatology, thus preventing timely recognition and treatment. Bubonic plague is highly treatable and curable with early antibiotic intervention, reducing mortality rates from over 50% to less than 5%. Prompt administration of antibiotics like streptomycin, gentamicin, or doxycycline is crucial, ideally within 24hr of symptom onset, usually requiring hospitalization.

Acknowledgment

The authors thank the Saastra College of Pharmaceutical Education and Research, Nellore, A.P, India, for technical assistance and support.

Conflict of Interests

The authors declare no conflict of interest

Ethics Approval

Not applicable

Funding

This study received no specific funding from public, commercial, or not for profit funding agencies.

AI Tool Declaration

The authors declare that no AI and related tools are used to write the scientific content of this manuscript.

Data Availability

Data will be available on request

References

[1] Kelly J. HarperCollins; New York, NY: 2006. The Great Mortality. An Intimate History of the Black Death, the Most Devastating Plague of All Time; pp. 138–141. 1-77.

[2] Zietz BP, Dunkelberg H. The history of the plague and the research on the causative agent Yersinia pestis. Int J Hyg Environ Health. 2004; 207(2): 165–178.

[3] Narayanan N, Lacy CR, Cruz JE, et al. Disaster preparedness: biological threats and treatment options. Pharmacotherapy. 2018; 38(2): 217–234.

[4] Demeure CE, Dussurget O, Fiol GM, et al. Yersinia pestis and plague: an updated view on evolution, virulence determinants, immune subversion, vaccination, and diagnostics. Genes Immun. 2019; 20(5): 357–370.

[5] Dean KR, Krauer F, Walløe L, et al. Human ectoparasites and the spread of plague in Europe during the second pandemic. Proc Natl Acad Sci U S A. 2018; 115(6): 1304–1309.

[6] Jones SD, Atshabar B, Schmid BV, et al. Living with plague: lessons from the Soviet Union's antiplague system. Proc Natl Acad Sci U S A. 2019; 116(19): 9155–9163.

[7] Godfred-Cato S, Cooley KM, Fleck-Derderian S, et al. Treatment of human plague: a systematic review of published aggregate data on antimicrobial efficacy, 1939-2019. Clin Infect Dis. 2020; 70: S11–S19.

[8] Danforth M, Novak M, Petersen J, et al. Investigation of and response to 2 plague cases, Yosemite National Park, California, USA, 2015. Emerg Infect Dis. 2016; 22(12): 2045–2053.

[9] Migita K, Asano T, Sato S, et al. Familial Mediterranean fever: overview of pathogenesis, clinical features, and management. Immunol Med. 2018; 41(2):55–61.

[10] Park YH, Remmers EF, Lee W, et al. Ancient familial Mediterranean fever mutations in human pyrin and resistance to Yersinia pestis. Nat Immunol. 2020; 21: 857–867.

[11] Alfani G, Percoco M. Plague and long-term development: the lasting effects of the 1629-1630 epidemic on the Italian cities. Econ History Rev. 2019; 72(4): 1175–1201.

[12] Colet C, Santiveri MI, Xavier J, et al. The Black Death and its consequences for the Jewish community in Tarrega: Lessons from history and archeology. Medieval Globe. 2014; 1(1): 63–96.

[13] Cohn SK. Plague violence and abandonment from the Black Death to the early modern period. Annales de démographie historique. 2017; 134(2): 39–61.

[14] Perry RD, Fetherston JD. Yersinia pestis-etiologic agent of plague. Clin Microbiol Rev. 1997; 10(1): 35–66.

[15] Kugeler KJ, Staples JE, Hinckley AF, et al. Epidemiology of human plague in the United States, 1900-2012. Emerg Infect Dis. 2015; 21(1):16–22.

[16] Butler T. Review article: plague gives surprises in the first decade of the 21st century in the United States and worldwide. Am J Trop Med Hyg. 2013; 89(4):788–793.